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Clinico-seroepidemiological evaluation of toxocariasis in asthmatic pediatric children in Mansoura city in Egypt

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Abstract

Background: Toxocariasis is a zoonotic geo-helminthes infection with reactive respiratory changes occurring in response to its larval migration. The aim of this study was to determine the *Toxocara* seropositivity in asthmatic children and to assess its relation to clinical signs, laboratory tests and epidemiological risk factors.

Methods and findings: 120 asthmatic and 60 non-asthmatic children were included in the study. The anti-*Toxocara* IgG antibodies were investigated in all serum samples using ELISA. The *Toxocara* seropositivity was significantly higher in asthmatic group than the control one; 84% and 16%, respectively. There was significant difference between both groups regarding IgE level, eosinophilia, geophagia, splenomegaly and hepatomegaly with no significant difference as regard gender, locality, lymphadenopathy and contact with pets.

Conclusion: *Toxocara* infection should be considered as a potential environmental risk factor inducing asthma among children population in developing countries.

Introduction

Toxocariasis is one of the most commonly reported zoonotic helminthes infection in the world recorded in both developing countries; where it is usually associated with low socioeconomic level [1], and developed countries, especially in rural areas among children who have pets [2, 3]. Toxocariasis seroprevalence has been reported to fluctuate between 2 and 92.8% according to geographical region and age group [4, 5].

Human infection occurs by accidental ingestion of embryonated eggs of *Toxocara canis* or *Toxocara cati*, the intestinal parasites of dogs and cats, respectively [6] where only few larvae are needed to cause disease [7]. Contact with contaminated soil is considered to be the primary route of transmission of *Toxocara* in humans [8], in addition to, direct contact with dog carrying eggs in their fur [9]. Other methods of transmission include: geophagia, poor personal hygiene as well as consumption of raw vegetables grown in contaminated gardens [10].

Migration of infected larvae through the human tissues, in the majority of cases does not result in clinical manifestation [11]. However, in parasitized individuals with the presence of anti-*Toxocara* antibodies visceral larva migrans is induced (VLM), which affects mainly young children and characterized by leukocytosis, fever, hepatomegaly, hypergammaglobulinemia, coughing, wheezing, abdominal pain, and elevated serum IgE level [12, 13]. Eosinophilia is one of the most outstanding characteristic of the VLM in naturally infected humans and experimental models of infection [3, 8].

Human toxocariasis is still a poorly diagnosed disease hence largely unknown either to health professionals and/or the general of Egyptian population [6]. It's difficult to be diagnosed by the direct techniques thus ELISA is used most often in diagnosis and during epidemiologic studies. ELISA has high sensitivity and specificity with insignificant levels of cross-reactivity reported when the excretory and secretory antigens of the *T. canis* larvae second-stage are used [14, 15].

Asthma is considered the most common chronic disease of childhood [16]. Atopy is an important risk factor for asthma, since about half of asthma cases are atopic individuals [17] as refereed by the collected epidemiological records which suggested that *Toxocara* infection had contributed significantly in the pathogenesis of atopy [18]. Most previous studies revealed no association between toxocariasis and asthma [19] but positive correlation was proved by other studies [20, 21].

Due to these controversy results, the present study aimed to investigate the *Toxocara* seropositivity in asthmatic children, in our locality (Mansoura city, Egypt) and to record its association with clinical signs, laboratory tests and epidemiological factors.

Material and methods

Sampled participants

The study was carried out on asthmatic children attending Allergy and Immunology outpatient clinic at Mansoura University Children hospitals, Egypt during the period from January 2010 to January 2012. The study protocol was approved by the institutional committee for the protection of human subjects and the Ethics Committee of Faculty of medicine, Mansoura University. Asthma cases were diagnosed according to the GINA recommendations [17]. The controls were attendee of other outpatient clinics with no respiratory complaint. Their age range was from 2 to 15 years. A questionnaire forms were prepared and given to parents of each case within both groups. The questionnaire contained epidemiological data including: age, sex, address (either urban or rural), geophagia and contact with pets, were recorded in a preplanned sheet format and then the child was subjected to full physical examination. It worth to be mentioned that the exclusion criteria among the studied population was for all cases positive for nematodes infection by stool examination (eg, ascariasis, enterobiasis, strongyloidiasis and trichostrongyliasis) to overcome cross reactivity with toxocariasis.

Sample collection

Five ml of venous blood was collected from each child placed in 2 tubes, one containing anticoagulant for CBC with differential leukocytes count. Especially looking for those with Eosinophilia corresponded to levels above 400/ mm^3 [3]. The blood sample in the second tube is centrifuged then collected serum was divided into two tubes, one for *Toxocara* serology and the other for measurements of total IgE. Serum samples were stored at –20°C until used. Stool samples were also obtained from all enrolled children and examined. Positive cases for other nematode infection were excluded to eliminate possible cross-reactions.

Serological investigation

Serum samples were tested for both anti-*Toxocara* IgG and IgE antibodies. The IgG detection was done using RIDASCREEN *Toxocara*-IgG ELISA kit (R-Biopharm AG, Germany) which detect antibodies against the excretory/secretory antigen of the *T. canis* larvae. While quantitative determination of total IgE antibodies concentration was carried out by IgE ELISA kit (Immunospec corporation, CA), where levels above 200 IU/ml were considered high. In both procedures, the manufacturer's guidelines were followed. Before testing for anti-*Toxocara* IgG antibodies serum samples were pre-incubated with *Ascaris* antigen to avoid immunologic cross-reactivity between *Toxocara* and *Ascaris*.

Statistical analysis

All data were introduced in an Excel spreadsheet and statistical analysis was carried out using the SPSS statistical package version 16 (SPSS, Inc., Chicago, IL, USA). Chi-square test and Odds Ratio (OR) were performed to confirm the difference between groups. The level of significance selected was p value < 0.05.

Results

The total of 120 asthmatic children besides 60 non-asthmatic controls, were included in the study. The age (mean±SD) of asthmatic group and control one were (5.73±3.493) and (6.01±3.048), respectively, with no significant difference between both groups (P>0.05). Regarding the clinical and epidemiological factors, there was significant difference between asthmatic group and control group regarding geophagia, splenomegaly and hepatomegaly (P<0.05) but as regard gender, locality, lymphadenopathy and contact with pets there was no difference between both groups (P>0.05), as shown in (**Table 1**). Concerning the laboratory investigations, significant difference was detected between asthmatic and control group regarding IgE level, anti- *Toxocara* IgG and eosinophilia (**Table 2**).

Table 1. Clinical and epidemiological factors recorded in the study groups.

	Asthmatic group n (%)	Control group n (%)	Odds ratio (95% CI)	*P* Value
Gender				
Male	67 (72%)	26 (39.1%)	1.398 (920-2.125)	0.114
Female	53 (60.9%)	34 (39.1%)		
Contact with pets				
No	67 (61.5%)	42 (38.5%)	1.520 (.955-2.418)	.0670
Yes	53 (74.6%)	18 (25.4%)		
Geophagia				
No	79 (60.8%)	51 (39.2%)	2.179 (1.162-4.089)	.0070
Yes	41 (82.0%)	9 (18.0%)		
Locality				
Urban	56 (62.2%)	34 (37.8%)	0.765 (.503-1.162)	.2060
Rural	64 (71.1%)	26 (28.9%)		
Liver				
Normal	72 (58.5%)	51 (41.5%)	2.626 (1.391-4.957)	.0010
Enlarged	48 (84.2%)	9 (15.8%)		
Spleen				
Normal	82 (58.6%)	58 (41.4%)	8.286 (2.116-32.448)	.0010
Palpable	38 (95.0%)	2 (5.0%)		
Lymph nodes				
Normal	71 (61.7%)	44 (38.3%)	1.554 (.957-2.524)	.0620
Enlarged	49 (75.4%)	16 (24.6%)		

Table 2. Laboratory findings in the study groups.

	Asthmatic group n (%)	Control group n (%)	Odds ratio (95% CI)	P Value
Eosinophiles				
Within normal limits	80 (60.6%)	52 (39.4%)	2.364 (1.213-4.605)	.0040
High	40 (83.3%)	8 (16.7%)		
IgE				
Within normal limits	38 (40.0%)	57 (60.0%)	17.000 (5.527-52.285)	.0010
Elevated	82 (96.2%)	3 (3.8%)		
ELISA (for anti-Toxocara IgG)				
Negative	78 (60%)	52 (40%)	2.500 (1.280-4.881)	.0020
Positive	42 (84%)	8 (16%)		

DiscussionAsthma has increased in industrialized countries recently [22]. Geohelminthes infection is considered as a potential environmental risk factor for asthma [23, 24]. Reactive respiratory changes occur in VLM, caused by *Toxocara* infection, because of larval migration and infected individuals are more likely to wheeze in response to larval invasion [13]. Studies on the association between *Toxocara* seropositivity and asthma have provided conflicting evidence with some showing positive association in human [20, 21] and in animal model [25], while others shown no relation [19]. This case-control study aimed to investigate *Toxocara* seropositivity in our locality (Mansoura city, Egypt), as a developing country, among asthmatic children as they are more prone to infection.

Our result demonstrated a positive association between asthma and *Toxocara* seropositivity which was concordant with cross-sectional study of children carried out in The Netherlands that demonstrated occurrences of asthma/recurrent bronchitis significantly associated with *Toxocara* seroprevalence [20]. Ferreira et al. (2007) carried their study among under-five Amazonian children demonstrated that 21.5% of examined children had antibodies to *Toxocara* and the increased risk of asthma was independently associated with seropositivity to *Toxocara* [21]. Our results agree with previous observations of higher *Toxocara* seropositivity rates in asthmatic children [26]. Contrarily, Sharghi et al. [19] didn't find any association between *Toxocara* seropositivity and asthma among 95 asthmatic and 229 non asthmatic children which was attributed to the lower number of asthmatic cases in that study.

There is a significant relation between *Toxocara* infection and geophagia in the present study. Previous studies reported that geophagia is an important risk for *Toxocara* infection [20, 27]. In our locality, infection can occur in both urban and rural areas due to contact with *Toxocara* ova contaminating ground from stray infected dogs or contact with domestic pets, respectively.

We have observed that the reported clinical signs suggestive of toxocariasis have a correlation with positive *Toxocara* serology. This is in accordance with the previous results of Teixeira et al. [28] who founded that children with seroprevalence for *Toxocara* have a significant relation to enlarged liver and spleen (p= .0010). Other studies reported that toxocariasis should be considered in differential diagnosis of eosinophilia, in patients with bronchospasms, isolated hepatomegaly and splenomegaly [29]. It was stated that *T. canis* infection must be considered in at-risk children, such as those with puppies at home, who have had contact with soil, who have hepatomegaly and/or asthma with eosinophilia and increased serum IgE [30]. Bahnea et al., reported that the most frequent clinical manifestation was pulmonary symptoms and the most frequent digestive symptoms were abdominal pain and hepatosplenomegaly in adult with positive anti-*Toxocara* antidodies. The laboratory diagnosis of their study population revealed, hypereosinophilia in 94.73% childrens associated with hyperleucocytosis and hyper-gamma globulinemia. All the patients were serologically confirmed with toxocariasis [31].

In the present work, a statistical significance between the asthmatic group and the control group regarding eosinophilia, IgE and anti –*Toxocara* IgG (p= 0.004, 0.001, 0.002 respectively) was detected. These results are in accordance with other studies suggesting that eosinophilia and increased serum IgE in asthmatic patients are highly suggestive of toxocariasis [29-31].

In conclusion, this study demonstrated a significant correlation between *Toxocara* seropositivity and bronchial asthma in pediatric asthmatic population in our locality emphasizing the role concerning *Toxocara* infection as an important environmental risk factor for asthma. It's important to high light this neglected parasite as a potential risk factor for asthma. Physicians should pay attention to incorporate toxocariasis in the differential diagnosis of asthma with hepatomegaly and splenomegaly.

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